Claims

1. A recombinant influenza virus for high-yield expression of incorporated foreign gene(s), which is genetically stable in the absence of any helper virus and which comprises at least one viral RNA segment being a bicistronic RNA molecule coding for two genes in tandem arrangement (tandem RNA segment), in said tandem RNA segment one of the standard viral genes being in covalent junction with a foreign, recombinant gene and said tandem RNA segment having an upstream splice donor and a downstream splice acceptor signal surrounding the proximal coding region.

2. The recombinant influenza virus of claim 1, wherein the tandem RNA segment contains one of the standard viral genes in distal mRNA position behind a foreign, recombinant gene in proximal position, or vice versa, both in antisense orientation with regard to the viral RNA as present within the virus.

3. The recombinant influenza virus of claim 1 or 2, wherein at least one of the regular viral RNA segments is replaced by a tandem RNA segment, preferably the replaced regular viral RNA segment is selected from the neuraminidase segment, hemaglutinin segment and NS segment.

4. The recombinant influenza virus of claims 1 to 3, wherein the splice donor and splice acceptor signals are selected from sequences as present in influenza WSN segment 7 and 8 or other partially effective splice reactin substrates.

5. The recombinant influenza virus of claim 4, wherein the splice donor and splice acceptor signals are selected from sequences as present in influenza WSN segment 7.

6. The recombinant influenza virus according to claims 1 to 5, wherein one or more of the regular viral RNA segments, differing from said at least one tandem RNA segment, comprises a vRNA encoding a foreign gene which may or may not be in covalent connection to one of the viral genes, and preferably one or more of the regular viral RNA segments has (have) been deleted and replaced by a tandem vRNA encoding in addition a foreign gene.

7. The recombinant influenza virus according to claims 1 to 6, in which the terminal viral RNA sequences of one or more of the regular segments and/or of the at least one tandem RNA segment, which are active as the promoter signal, have been modified by nucleotide substitutions in up to five positions, resulting in improved transcription rates of both the vRNA promoter as well as the cRNA promoter as present in the complementary sequence.

8. The recombinant influenza virus of claim 7, wherein the 12 nucleotide conserved influenza 3' terminal sequence has been modified by replacement of one to three nucleotides occurring in said sequence at positions 3, 5 and 8 relative to the 3' end by other nucleotides, and/or wherein the 13 nucleotide conserved influenza 5' terminal sequence has been modified by replacement of one or two nucleotides occurring in said sequence at positions 3 and 8 by other nucleotides.

9. The recombinant influenza virus of claim 8, wherein the replacements in the 3' terminal nucleotide sequence comprises the modifications G3A and C8U.

10. The recombinant influenza virus of claim 9, wherein the replacements in the 3' terminal nucleotide sequence comprises the modifications G3A, U5C and C8U, or G3C, U5C and C8G.

11. The recombinant influenza virus of claim 10, which comprises a 3' terminal nucleotide sequence of (5')-CCUGUUUCUACU-3'.

12. The rcombinant influenza virus according to claims 7 to 12, wherein the 5' terminal nucleotide sequence comprises the modifications U3A and A8U resulting in a 5'-terminal sequence of 5'-AGAAGAAUCAAGG.

13. The recombinant influenza virus according to claims 1 to 12, which is a recombinant influenza A virus.

14. The recombinant influenza virus according to claims 1 to 13, in which the foreign gene(s) in the tandem RNA segment code for proteins and/or glycoproteins which are secreted from cells infected with the recombinant virus.

15. The recombinant influenza virus according to claims 1 to 13, in which the foreign gene(s) in the tandem RNA segment code for proteins or artificial polypeptides designed to support an efficient presentation of inherent epitopes at the surface of infected cells, for stimulation of a B cell and/or T cell response.

16. The recombinant influenza virus according to claims 1 to 13, in which the foreign gene(s) in the tandem RNA segment is a nucleotide sequence causing viral attenuation.

17. The recombinant influenza virus of claim 16, wherein the foreign gene is coding for part of or for the entire viral neuraminidase gene in antisense orientation.

18. The recombinant influenza virus of claim 17, wherein the neraminidase gene in antisense orientation is attached to the hemaglutinin vRNA

segment, and optionally another gene or reporter gene is encoded in a second tandem vRNA, preferably in conjunction with NS2.

19. A method for the production of recombinant influenza viruses as defined in claims 1 to 18 comprising

(a) RNA polymerase I synthesis of recombinant vRNAs *in vivo,* in antisense or in sense tandem design,

(b) followed by infection with an influenza carrier strain constructed to include flanking ribozyme target sequences in the corresponding viral RNA segment, and

(c) thereafter selective vRNA inactivation through ribozyme cleavage.

20. A pharmaceutical composition comprising a recombinant influenza virus according to claims 1 to 18, preferably a recombinant influenza virus of claims 16 to 18.

21. Use of a recombinant influenza virus according to claims 1 to 18, preferably a recombinant influenza virus of claims 16 to 18, for preparing a medicament for vaccination purposes.

22. The use according to claim 21, wherein the medicament

(a) is suitable against influenza and/or against other infections;

(b) is present in form of inactivated preparations; and/or

(c) is present in form of live recombinant viruses.

23. Use of a recombinant influenza virus according to claims 1 to 18 for preparing agents for somatic gene therapy.

24. Use of a recombinant influenza virus according to claims 1 to 18 for preparing agents, for transfer and expression of foreign genes into cells infected by such viruses.

25. Use of a recombinant influenza virus according to claims 1 to 18 for preparing agents for transfer and expression of RNA molecules into cells infected by such viruses.

26. The use of claim 24, wherein the RNA molecules to be expressed are antisense sequences or double-strand sequences relative to the target cell cellular mRNA molcules, and/or the agent is suitable for sequence-specific gene silencing, preferably by antisense RNA or RNA interference mechanisms.

27. The use according to claims 23 to 26, wherein the agents are applicable in *ex vivo* and *in vivo* application schemes.

28. A method for the production of proteins or glycoproteins which comprises utilizing a recombinant influenza virus according to claims 1 to 19 as expression vector.

29. The method of claim 28, wherein the production is performed in cell culture cells or in fertilized chicken eggs.

30. A method for preventing and/or treating influenza which comprises administering an effective amount of a recombinant influenza virus according to claims 1 to 18, preferably of a recombinant influenza virus according to claims 16 to 18, to the mammal to be treated.

31. A method for somatic gene therapy, which method comprises subjecting the organism to be treated with a recombinant influenza virus according to claims 1 to 18.

32. A method for transfer and expression of foreign genes into cells, and for transfer and expression of RNA molecules into cells, which method

comprises infecting the cells with a recombinant influenza virus according to claims 1 to 18.

33. Use of a recombinant influenza virus according to claims 1 to 18 for preparing agents for immunotherapy, preferably for autologous immunotherapy.

34. A method for an immunotherapy which comprises *ex vivo* infection of immune cells, preferably dentritic cells, with a recombinant influenza virus according to claims 1 to 18, and introduction of the transduced cells into the patient.

35. A method for the induction of antibodies which comprises utilizing a recombinant influenza virus according to claims 1 to 18 as an immunogen.